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Judi Bryant

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10/13/2006

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EXAMINER

BALASUBRAMANIAN, VENKATARAMAN

ART UNIT

PAPER NUMBER

1624

DATE MAILED: 10/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/722,591

Applicant(s)

BRYANT ET AL.

Examiner

Venkataraman Balasubramanian

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 July 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 3-12, 17-20 and 26-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 10 and 11 is/are allowed.
- 6) ☒ Claim(s) 3-9, 12, 17-20 and 26-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- ☐ Notice of Informal Patent Application
- ☐ Other: _____.

DETAILED ACTION

Applicants' response, which included amendment to claims 3-12 and 17-20, addition of claims 26-33 and cancellation of claims 1, 2, 13-16 and 21-25, filed on 7/20/2006, is made of record. Claims 3-12 and 17-20 and 26-33 are now pending.

In view of applicants' response, all 112 second and first paragraph scope of enablement rejections of related isotopes, prodrugs and solvates were deemed as obviated. However, the following rejections made in the previous office action are maintained and or applied to the newly added claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following apply. Any claim not specifically rejected is rejected as it dependent on a rejected claim and shares the same indefiniteness.

1. Recitation of "isotope" in claim 30 renders claim 30 and its dependent claims 31-33 indefinite, as it is not clear what are the isotopes and what is the structural make-up of the compound intended. Specification provides no definition of these related isotopes.
2. Recitation of "prodrug thereof" in claim 30 renders claim 30 and its dependent claims 31-33 indefinite. Prodrugs in general and as noted in specification, are compounds, which undergo in vivo hydrolysis to parent active drugs. In that sense

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recitation of prodrug is acceptable. However, the compound of formula I includes an amide group, and therefore it is not clear what is the difference between this amide group and the prodrug groups. There is clear-cut ambiguity as to what is to be considered as prodrug and what is not. Applicants should note that if the variable groups are prodrug, which are in general inactive but becomes active upon in vivo transformation, then the compound bearing the variable group would be deemed as inactive which is not what the claim recites.

Furthermore, the issue on second paragraph is whether the structures of the claimed compounds are clearly defined. Applicants' "prodrugs" are molecules whose structure lie outside the subject matter of formula (I), but upon metabolism in the body are converted to active compounds falling within the structural scope of formula (I). The claim describes the function intended but provides no specific structural guidance to what constitutes a "prodrug". Structural formulas, names, or both can accurately describe organic compounds, which are the subject matter of claim 1. Attempting to define means by function is not proper when the means can be clearly expressed in terms that are more precise.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making salts of the claimed compounds, does not reasonably provide enablement for making prodrug of the claimed compounds. The

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claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art of medicinal chemistry - to use the invention. "The factors to be considered in making an enablement rejection have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. a) Finding a prodrug is an empirical exercise. Predicting if a certain ester of a claimed alcohol, for example, is in fact a prodrug, and produces the active compound metabolically, in man, at a therapeutic concentration and at a useful rate is filled with experimental uncertainty. Although attempts have been made to predict drug metabolism 'de novo, this is still an experimental science. For a compound to be a prodrug, it must meet three tests. It must itself be biologically inactive. It must be metabolized to a second substance in a human at a rate and to an extent to produce that second substance at a physiologically meaningful concentration. Thirdly, that second substance must be biologically active. Thus, determining whether a particular compound meets these three criteria in a clinical trial setting requires a large quantity of experimentation.

There is no working example of a prodrug of a compound the formula (I). The nature of the invention is clinical use of compounds and the pharmacokinetic behavior of substances in the human body. The state of the prodrug art is summarized by Wolff (Medicinal Chemistry). The table on the left side of page 976 outlines the research

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program to be undertaken to find a prodrug. The second paragraph in section 10 and the paragraph spanning pages 976-977 indicate the low expectation of success. In that paragraph the difficulties of extrapolating between species are further developed. Since, the prodrug concept is a pharmacokinetic issue, the lack of any standard pharmacokinetic protocol discussed in the last sentence of this paragraph is particularly relevant. Banker (Modern Pharmaceuticals) in the first sentence, third paragraph on page 596 states that "extensive development must be undertaken" to find a prodrug. Wolff (Medicinal Chemistry) in the last paragraph on page 975 describes the artisans making Applicants' prodrugs as a collaborative team of synthetic pharmaceutical chemists and metabolism experts. All would have a Ph. D. degree and several years of industrial experience. It is well established that "the scope of enablement varies inversely degree of unpredictability of the factors involved", 'and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). h) The breadth of the claims includes all of the hundreds of thousands of compounds of formula of claim I as well as the presently unknown list potential prodrug derivatives embraced by the word "prodrug".

Thus, undue experimentation will be required to determine if any particular derivative is, in fact, a prodrug.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*,

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999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).” That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants’ invention.

Claims 30-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for making pharmaceutically acceptable salts does not reasonably provide enablement for making solvate and polymorph. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The following apply.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1. The nature of the invention and the state of the prior art:

The invention is drawn to compound of formula I, or a pharmaceutically acceptable salt, solvate or polymorph thereof. Specification is not adequately enabled as to how to make solvate and polymorph of compounds of formula (I) Specification has no example of solvate and polymorph of the instant compounds. Specification on page 5 recites solvate or polymorph thereof but there is no enabling of such compounds.

Search in the pertinent art, including water as solvent, resulted in a pertinent reference, which is indicative of unpredictability of solvate and polymorph formation in general. The state of the art is that is not predictable whether solvates or hydrates or polymorph will form or what their composition will be. In the language of the physical chemist, a solvate or hydrate of organic molecule is an interstitial solid solution. This phrase is defined in the second paragraph on page 358 of West (Solid State Chemistry). The solvent molecule is a species introduced into the crystal and no part of the organic host molecule is left out or replaced. In the first paragraph on page 365, West (Solid State Chemistry) says, "it is not usually possible to predict whether solid solutions will form, or if they do form what is the compositional extent". Thus, in the absence of experimentation one cannot predict if a particular solvent will solvate any particular crystal. One cannot predict the stoichiometry of the formed solvate, i.e. if one, two, or a half a molecule of solvent added per molecule of host. Compared with polymorphs, there is an additional degree of freedom to hydrates, which means a different solvent or even the moisture of the air that might change the stable region of the hydrate. In the instant case of hydrate a similar reasoning therefore apply. Water is a solvent and hence it is held that a pertinent detail of West, which relates to solvates, is also applicable to hydrate

In addition, an additional search resulted in Vippagunta et al., Advanced Drug Delivery Reviews 48: 3-26, 2001, which clearly states that formation of polymorphs hydrates and solvates is unpredictable. See entire document especially page 18, right column section 3.4. Note Vippagunta et al., states "Each solid compound responds

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uniquely to the possible formation of solvates or hydrates and hence generalizations cannot be made for series of related compounds". See page 11 for polymorphs.

2. The predictability or lack thereof in the art:

Hence, the solvate and polymorph as applied to the above-mentioned compounds claimed by the applicant are not art-recognized compounds and hence there should be adequate enabling disclosure in the specification with working example(s).

3. The amount of direction or guidance present:

Examples illustrated in the experimental section are limited to making the compounds not related to solvates and polymorphs. There is no example of a solvate or polymorph of instant compound. Over eight hundred and eighty one compounds were shown in the examples of the specification each of which has come in contact with water and other solvent but there is no showing that instant compounds formed solvates or hydrates or polymorphs. Hence it is clear that merely bring the compound with solvent or water does not result in solvate or hydrate or polymorph and additional direction or guidance is needed to make them. Specification has no such direction or guidance.

4. The presence or absence of working examples:

There is no working example of any solvate or polymorph formed. The claims are drawn to solvate and polymorph, yet the numerous examples presented all failed to produce a solvate or polymorph. These cannot be simply willed into existence. As was stated in *Morton International Inc. v. Cardinal Chemical Co.*, 28 USPQ2d 1190 "The

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specification purports to teach, with over fifty examples, the preparation of the claimed compounds with the required connectivity. However ... there, is no evidence that such compounds exist... the examples of the '881 patent do not produce the postulated compounds... there is ...' no evidence that such compounds even exist." The same circumstance appears to be true here. There is no evidence that hydrates of these compounds actually exists; if they did, they would have formed. Hence, there should be showing supporting that solvates and polymorphs of these compounds exist and therefore can be made.

5. The breadth of the claims & the quantity of experimentation needed:

Specication has no support, as noted above, for compounds generically embraced in the claim 30 would lead to desired solvate or polymorph of the compound of formula I. The quantity of experimentation needed would be an undue burden on skilled art in the chemical art since there is inadequate guidance given to the skilled artisan for the many reasons stated above. Even with the undue burden of experimentation, there is no guarantee that one would get the product of desired solvate or polymorph of compound of formula I embraced in the instant claims in view of the pertinent reference teachings.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is

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clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

Claims 30-33 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compound of formula I, does not reasonably provide enablement for compound of formula I with isotopes. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The following apply:

In evaluating the enablement question, following factors are considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1. The nature of the invention and the state of the prior art:

The invention is drawn to a compound of formula I and as well as compound of formula I with related isotopes. As recited, first of all, the related isotopes remain unknown and the term reads on any or all isotopes of elements known. As recited instant claims are reach thorough claims wherein based on the fact that a there are isotopes, it is claimed that the compound of formula I can have any or all isotopes known. In addition, it is also implied that the compounds derived from such related isotopes would also share the same utility for which there is no enabling disclosure in the specification.

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Specification is silent about the choice of related isotopes or the nature of these isotopes.

Isotope labelling in general is a specialized art. Particularly radiolabelling with positron emitters is much more specialized art due time constrain imposed by the short half-life the positron emitters. Careful design and performance of synthesis of suitable precursor is needed not only to rapidly make the labeled compound but also to separate starting precursor from the desired final product. A reaction, which works for a particular precursor, may not work for other precursor. The art is not predictable. Thus the breadth of the instants claims which is broad to include any available position for ^{11}C labeling and use of the resultant compound lacks adequate support in the specification. The same is true for various other radiolabels or isotope where one need design and develop a process for each compound. See Pimlott SL., Nucl. Med. Commun. 26(3): 183-188, 2005 (PubMed Abstract provided).

2. The predictability or lack thereof in the art:

Hence the process as applied to the above-mentioned isotopically labeled compounds claimed by the applicant with any isotopes is not art-recognized process and hence there should be adequate enabling disclosure in the specification with working example(s) to make the compound of formula I with related isotopes claimed.

4. The amount of direction or guidance present:

Examples illustrated in the experimental section or written description offer no guidance or teachings as to the process of making compound of formula I wherein the with related isotopes but and those examples shown cannot be deemed as objective

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enablement for any isotope and one need to search for such isotope as there is no guidance provided in the specification for such selection of suitable isotope and the process of making them.

5. The presence or absence of working examples:

Although examples show the instant compounds, as noted above, they are limited to process of making compound of formula I with hydrogen, carbon, nitrogen and oxygen. There are no representative examples showing the viability of the process for plurality of isotopes generically embraced in the instant claim.

6. The breadth of the claims:

Specification has no support, as noted above, for all reducing agents and there is no guidance as to what is suitable for such a process and there is also no valid chemical reasoning for one trained in the art to expect that all isotopes would be applicable and share the same use embraced.

7. The quantity of experimentation needed:

The quantity of experimentation needed would be an undue burden on skilled art in the chemical art since there is inadequate guidance given to the skilled artisan for the many reasons stated above. Even with the undue burden of experimentation, there is no guarantee that one would get the product of desired structure, namely compound of formula I embraced in the instant claims.

Thus, factors such as "sufficient working examples", the "level of skill in the art and predictability, etc. have been demonstrated to be sufficiently lacking in the case for the instant claims.

Claims 17-20, 27 and 28 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating rheumatoid arthritis does not reasonably provide enablement treating or preventing any or all cancer, any or all autoimmune disease, any or all cardiovascular disease, any or all infectious diseases, any or neurodegenerative disease, any or all eye disease and various other diseases, embraced in the instant invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims for reasons of record. To repeat: Following apply.

Method of use claims 17-20, 27 and 28 and 25 recite treating cancer in general and solid tumor in specific for which there is no adequate written description and enabling disclosure in the specification.

As recited, claims 17-20, 27 and 28 are reach through claims. Reach through claims, in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through any or all diseases, disorders or conditions for which they lack written description and enabling disclosure in the specification. In the instant case, because of inhibition of kinase activity in general or more specifically inhibition of Akt, Pdk, chk and or VEGF-R activity by compound formula I, it is recited that instant compounds are useful for treatment of any or all disease stated above for which there is no adequate written description and enabling disclosure in the instant specification.

The scope of the claims includes treating any or all cancer, any or all proliferative diseases, any or all autoimmune disease, any or all cardiovascular disease, any or all infectious diseases, any or neurodegenerative disease, any or all eye disease and various other diseases due to Akt, Pdk, chk and or VEGF-R kinase inhibition including those yet to be discovered as due said mode of action for which there is no enabling disclosure. From the reading of specification, it appears that the applicants are asserting that the embraced compounds because of their mode action, which involves inhibition of to Akt, Pdk, chk and or VEGF-R kinases, would be useful for treating the above said diseases or disorders. The scope of the is not adequately enabled solely based on the activity of the compounds as kinase inhibitors provided in the specification at pages 55-64. Moreover many if not most of diseases such as psoriasis, lung cancer, brain cancer, pancreatic cancer, colon cancer etc., are very difficult to treat despite the fact that there are many anticancer drugs and inflammatory drugs. The fact that there are number of such drugs available and that they have not been able to treat effectively or prevent contradicts instant invention.

The scope of the claims involves millions of compounds of claim 1 as well as the thousand of diseases embraced by the term cancer.

Proliferative disease would include benign tumors, malignant tumors, polyps, lumps, lesions, other pre-cancerous conditions, psoriasis, leukemia, the hyper proliferation of the gastric epithelium caused by the *Helicobacter pylori* infection of ulcers.

Cancer is just an umbrella term. Tumors vary from those so benign that they are never treated to those so virulent that all present therapy is useless.

No compound has ever been found to treat proliferative diseases of all types generally. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The existence of such a "compound" is contrary to our present understanding of oncology. Cecil Textbook of Medicine states, "each specific type has unique biologic and clinical features that must be appreciated for proper diagnosis, treatment and study" (see the enclosed article, page 1004). Different types of cancers affect different organs and have different methods of growth and harm to the body. Thus, it is beyond the skill of oncologists today to get an agent to be effective against cancers generally. Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See *Ex parte Jovanovics*, 211 USPQ 907, 909; *In re Langer* 183 USPQ 288. Also note *Hoffman v. Klaus* 9 USPQ 2d 1657 and *Ex parte Powers* 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Utility and Written Description Guidelines, at 66 FR 1092-1099, 2001 wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method of treating solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See *Mass, R. D.*, *Int. J. Radiation Oncology*

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Bio. Phys.Vol. 58(3): 932-940, 2004, Fabbro et al. Pharmacology & therapeutics 93, 79-98, 2002 and Tas et al., Curr. Pharm. Des. 11(5): 581-611, 2005.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

- 1) The nature of the invention: Therapeutic use of the compounds in treating any or all cancer that require receptor Akt, Pdk, chk and or VEGF-R kinase inhibitory activity.
- 2) The state of the prior art: Recent publications expressed that the receptor kinase inhibition effects are unpredictable and are still exploratory. See Mass et al. and Fabbro et al., cited above especially the concluding paragraph.
- 3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for treating any or all cancer due to Akt, Pdk, chk and or VEGF-R kinase inhibition of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).
- 4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples to show treating any or all

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cancers or abnormal cell growth and the state of the art is that the effects of Akt, Pdk, chk and or VEGF-R kinase inhibitors are unpredictable.

6) The breadth of the claims: The instant claims embrace any or all proliferative diseases and cancers including those yet to be related to Akt, Pdk, chk and or VEGF-R kinase.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as “sufficient working examples”, “the level of skill in the art” and “predictability”, etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of enzyme-inhibitor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards treating and preventing the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP §2164.01(a) states, “A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993).” That conclusion

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is clearly justified here and undue experimentation will be required to practice Applicants' invention.

This rejection is same as made in the previous office action but now limited pending method of use claims and cancer.

Applicants' argument to overcome this rejection is not persuasive.

First of all, as noted above, these claims are reach through claims. based on the mode of action these claims reach through treating any or all cancer including solid tumors for which there is no enabling disclosure.

Secondly, prior art does not teach that any known anti-cancer can be used to treat any or all cancer.

Applicants' have not provided any non-patent literature to support specific cancers claimed.

Hence, this rejection is deemed as proper and is maintained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 2, 12, 19-23 and 25 rejected under 35 U.S.C. 102(e) as being anticipated by Dahmann et al. US 2003/0171359.

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Dahmann et al. teaches several 2,4,5-trisubstituted pyrimidines as kinase inhibitors useful for treating arthritis, which include instant compounds. See page 2, formula I. note the definition of various variable groups. Especially note the R_aNR_b definition overlaps with instant aniline group, R_cNR_d overlaps with instant $X-R^2$ and the R_e choices includes instant R_1 choices. Thus with the given definition of these groups, compounds taught by Dahmann et al. include instant compounds. See entire document for details of the invention. Particularly see pages 23-86 for large number of compounds. Especially see example 1, which include several instant compounds.

Applicants' have not addressed this rejection directly in their response. Example 1 on page 32 has several compounds which would meet the R_1 , R_2 , A and b choices.

A response is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3-9, 12, 17-20 and 26-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Dahmann et al. US 2003/0171359.

As noted above, Dahmann et al. teaches several 2,4,5-trisubstituted pyrimidines as kinase inhibitors useful for treating arthritis, which include instant compounds. See page 2, formula I. note the definition of various variable groups. Particularly see pages 23-86 for large number of compounds Especially see example 1, which include several instant compounds.

Dahmann et al. differs in not exemplifying all compounds generically embraced in the formula I shown in page 2.

However, Dahmann et al. teaches equivalency of those compounds taught in pages 23-86 with those generically recited in for compound of formula I in pages 1-20.

Thus it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds using the teachings of Dahmann et al.

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and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

This rejection is same as made in the previous office action but now applied to pending claims. As for applicants request, example 1 on page 31-60 includes several compounds which would meet the limitations of instant claims. See for example entry 7 on page 32.

Hence, this rejection is deemed as proper and is maintained.

Allowable Subject Matter

Claims 10 and 11 are allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).


Venkataraman Balasubramanian

10/1/2006